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caps.

C What is claimed is: ³⁰
CLAIMS

1. A method for transforming a lymphoid cell line to glutamine independence which comprises:
transforming the lymphoid cell line with a vector
5 containing an active glutamine synthetase (GS) gene;
growing the transformed cell line on a medium containing glutamine; and
continuing the growth of the transformed cell line on a
medium in which the glutamine is progressively depleted or
10 on a medium lacking glutamine.
2. The method of claim 1, wherein the lymphoid cell line is a myeloma cell line.
- 15 3. The method of claim 1 or claim 2, wherein the glutamine-depleted or glutamine-free medium contains asparagine.
4. The method of any one of claims 1 to 3, wherein the
20 lymphoid cell line is transformed with a vector containing both an active GS gene and a gene encoding another selectable marker, such as a gpt gene, or cotransformed with separate vectors encoding GS and the selectable marker
respectively.
- 25 5. The method of any one of claims 1 to 4, wherein the glutamine in the medium is progressively depleted by dilution with a medium containing asparagine but lacking glutamine.
- 30 6. The method of any one of claims 1 to 5, wherein the vector used to transform the lymphoid cell line also contains an active gene coding for a protein heterologous to the lymphoid cell line.
- 35 7. The method of any one of claims 1 to 6, wherein the lymphoid cell line is co-transformed with a separate vector containing the active gene coding for the heterologous protein.
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8. The method of claim 6 or claim 7, wherein the heterologous protein is an Ig-type molecule.

9. The method of any one of claims 6 to 8, wherein the
5 GS gene comprises a relatively weak promoter and the gene
(or genes) encoding the heterologous protein comprises a
relatively strong promoter so that in the transformed cell
lines, protein synthesis is directed preferentially to the
production of the heterologous protein or peptide rather
10 than to the production of GS.

10. A vector for transforming a lymphoid cell line to
glutamine independence and to enable it to produce a
heterologous protein, the vector comprising a GS gene and a
15 gene encoding the heterologous protein, wherein the vector
is arranged such that expression of the GS gene is not
hindered by transcriptional interference from the
promoter/enhancer transcribing the coding sequence for the
heterologous protein to such an extent that glutamine-
20 independent colonies cannot be produced.

11. The vector of claim 10, wherein the GS gene contains
a relatively weak promoter, the gene encoding the
heterologous protein contains a relatively strong promoter,
25 and the promoter of the GS gene is located upstream of or
directs expression in the opposite direction to that of the
gene encoding the heterologous protein.

12. The vector of claim 11, wherein the combination for
30 the weak and strong promoters is the SV40 early region and
the hCMV-MIE promoters.

13. The vector of claim 10 or claim 11, wherein the vector
comprises a GS gene having a weak promoter having downstream
35 therefrom a heavy chain like gene having a strong promoter,
there being on the vector a light chain like gene having a
strong promoter oriented in the opposite direction to the
promoters of the GS and heavy chain like genes.

40 14. The vector of claim 10 or claim 11, wherein the GS

gene has a weak promoter, the vector contains a light chain like gene and a heavy chain like gene, the heavy and light chain like genes have strong promoters, the three genes are transcribed in the same direction and the GS gene is 5 upstream of the other two genes.

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B1

add C7

add D6